IN THE UNITED STATES PATENT & TRADEMARK OFFICE

In re Application of TORMO I BLASCO et al.

Serial No. 10/532,719

Filed: December 20, 2005

For: 6-(Halogenphenyl)-Triazolopyrimidines Derivatives and their use as Fungicide

DECLARATION

I, Egon Haden, Dr. agr., a citizen of th Federal Republic of Germany and residing at Römerstrasse 1, 67259 Kleinniedesheim, Germany, hereby declare as follows:

I am fully trained agricultural engineer, having studied agricultural science at the Technical University of Stuttgart-Hohenheim, Germany, from 1975 to 1980;

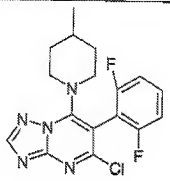
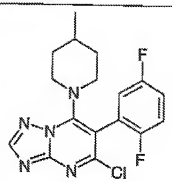
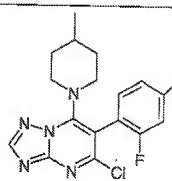
From 1980 to 1985 I furthered my studies at the Institute of Plant Disease of the University of Hohenheim, and I was awarded my doctor's degree by the said university in 1985;

I joined BASF Aktiengesellschaft of 67056 Ludwigshafen, Germany, in 1984, and have since been working in the field of the characterization and screening of fungicidal substances, and am therefore fully conversant with the technical field to which the invention disclosed and claimed in Application Serial No. 10/532,719 belongs.

I have read the application and studied the application file, in particular the Office Action dated August 21, 2007, and the prior art referenced therein, and I am therefore also well acquainted with the invention, which is disclosed and claimed in application 10/532,719.

The following tests were carried out under my supervision or the supervision of my colleagues in accordance with the procedures described on pages 39 to 41 and 26 to 29 of the application. I have reviewed the test protocols and based on my review and knowledge I consider those data to be fully reliable:

A. Comparative Tests

D2 (US 5,593,996) Ex. 119 Comparative Example	US Serial No. 10/532,719 Ex. I-44 Invention	US Serial No. 10/532,719 Ex. I-23 Invention
		

The active ingredients were used separately to prepare a stock solution comprising 25 mg active ingredient, which was filled up with a mixture of acetone and/or DMSO and the emulsifier Uniperol® EL (emulsifying and dispersing wetter based on ethoxylated alkylphenols) in a volume ratio solvent : emulsifier of 99 : 1 ad 10 ml solution. Afterwards water was added ad 100 ml. This stock solution was diluted with the above described solvent: emulsifier : water mixture to give the desired active ingredient concentrations stated below.

Comparative Test 1:

Control of gray mould (*Botrytis cinerea*) on paprika leaves in a seven day protective application

Paprika seedlings of the "Neusiedler Ideal Elite" variety were sprayed to run-off at the four- to five leave stage with an aqueous suspension containing the concentration of active ingredient mentioned below. After seven days the plants were inoculated with a spore suspension of *Botrytis cinerea* containing 1.7 x 10^6 spores per ml in 2 wt.-% aqueous biomalt solution. The infected plants were then incubated in chambers with high humidity for five days at 22-24 °C. The extent of fungus spread was assessed as %-attack of the whole leaf surface, which made it possible to judge not only the fungicidal action of the active ingredient but also the long term effect.

In this test, the plants which had been treated with 250 ppm of the comparative compound from D2 showed an infection of 50 %, while with 250 ppm of the inventive compound I-23 no infection could be detected. The untreated plants showed an infection of 90 %.

Comparative Test 2:

Action on *Pyricularia oryzae* (protective action)

Leaves of pot grown rice seedlings of the "Tai-Nong 67" variety were sprayed to runoff with an aqueous suspension, containing the concentration of active ingredient mentioned below. The next day the plants were inoculated with an aqueous spore suspension of *Pyricularia oryzae*. The plants were then placed for 6 days in a humid chamber at 22 to 24 °C and a relative humidity of 95 to 99 %. The extent of fungus spread was assessed as %-attack of the whole leaf surface.

In this test, the plants which had been treated with 250 ppm of the compound of D2 showed an infection of 80 %, whereas with 250 ppm of the inventive compounds I-23 and I-44 only 3 %, respectively 0 % infection could be detected. The untreated plants were infected to 90 %.

Comparative Test 3:

Action on *Septoria tritici* in wheat (protective action)

Leaves of pot grown wheat seedlings of the "Riband" variety were sprayed to runoff with an aqueous suspension, containing the concentration of active ingredient mentioned below. The next day the plants were inoculated with an aqueous spore suspension of *Septoria tritici* containing 2.0 x 10^6 spores/ml. The plants were then placed in a humid chamber at 18 to 22 °C and a relative humidity of almost 100 %. After two weeks the extent of fungus spread was assessed visually as %-attack of the whole leaf surface.

In this test, the plants which had been treated with 16 ppm of the compound of D2 showed an infection of 60 %, whereas with 16 ppm of the inventive compound I-23 no infection could be detected. The untreated plants were infected to 90 %.

The comparative test results clearly demonstrate that the tested compounds according to Appl. Ser. No. 10/532,719 have distinct advantages and improved fungicidal efficacy compared to example 119 of US 5,593,996.

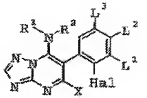
The tested compounds according to Appl. Ser. No. 10/532,719, which have a halogen atom in the 2-position of the phenyl ring, are unsubstituted in the 6-position and carry a further halogen substituent, show a markedly higher activity against gray mould on paprika leaves caused by Botrytis cinera, rice blast caused by Pyricularia oryzae and Septoria leaf blotch caused by Septoria tritici than the tested compound according to US 5,593,996 which has a substituent in the 2- and 6-position of the phenyl ring, but otherwise has the same structure as the compounds of Appl. Ser. No. 10/532,719.

B. Additional Examples

B1 Synthesis Examples

With due modification of the starting compounds, the protocols shown in the synthesis examples of US Serial No. 10/532,719 were used for obtaining further compounds I. The resulting compounds I, together with physical data, are listed in the following supplement to Table (I) in the specification of US Serial No. 10/532,719.

Additional Synthesis Examples
Table I



No.	R^1 — R^2	Hal	L^1	L^2	L^3	X	Phys. Data (mp. [°C])
I-182	$-CH(CH_3)(CH_2)_3-$	F	F	H	H	Cl	160-161
I-183	$-CH(CH_3)(CH_2)_4-$	F	F	H	H	Cl	169-172
I-184	$-(CH_2)CH(CH_3)(CH_2)_5-$	F	F	H	H	Cl	153-155
I-185	$-(CH_2)C(CH_3)_2(CH_2)_3-$	F	F	H	H	Cl	161-165
I-186	$-(CH_2)_5-$	F	F	H	H	Cl	172
I-187	$-CH(CH_2)(CH_2)_3-$	F	H	H	F	Cl	175-176
I-188	$-(CH_2)_5-$	F	H	H	F	Cl	158-159
I-189	$-(CH_2)CH(CH_3)(CH_2)_3-$	F	H	H	F	Cl	164-165
I-190	$-(CH_2)_2S(CH_2)_2$	F	H	H	F	Cl	213-215
I-191	$-CH(CH_3)(CH_2)_4-$	F	H	F	F	Cl	183-185
I-192	$-CH(CH_2)(CH_2)_4-$	F	H	F	H	Cl	180
I-193	$-CH(CH_3)(CH_2)_4-$	F	F	F	H	Cl	165
I-194	$-(CH_2)_2CH(CH_3)(CH_2)_2-$	F	F	H	F	Cl	170-172
I-195	$-(CH_2)_2CH(CH_3)(CH_2)_2-$	F	H	F	H	Cl	203-204
I-196	$-(CH_2)_2C(CH_3)=CH(CH_2)-$	F	H	F	H	Cl	193-194
I-197	$-(CH_2)_2CH(CH_3)(CH_2)_2-$	Cl	H	F	H	CH_3	235-237
I-198	$-(CH_2)_2CH(CH_3)(CH_2)_2$	Cl	H	F	H	CN	78-80
I-199	$-(CH_2)_2CH(CH_3)(CH_2)_2-$	Cl	H	F	H	OCH_3	185-187

No.	R^1 R^2	Hal	L^1	L^2	L^3	X	Phys. Data (mp. [°C])
I-200	-$(CH_2)CH(CH_3)(CH_2)_2$-	F	H	F	H	Cl	75-76
I-201	-$(CH_2)CH(CH_3)(CH_2)_2$-	Cl	H	F	H	Cl	142-144
I-202	-$(CH_2)_2C(CH_3)$=$CH(CH_2)$-	Cl	H	F	H	Cl	209-210
I-203	-$(CH_2)_2CH(CH_3)(CH_2)_2$-	F	H	H	F	Cl	178-180
I-204	-$(CH_2)_2CH(CH_3)(CH_2)_2$-	F	F	H	H	Cl	205-207
I-205	-$(CH_2)_2CH(CH_3)(CH_2)_2$-	Cl	H	H	F	Cl	187-189
I-206	-$(CH_2)CH(CH_3)(CH_2)_2$-	Cl	H	H	F	Cl	128-129
I-207	-$(CH_3)_2CH(CH_2)(CH_2)_2$-	Cl	H	H	Cl	Cl	186-187
I-208	-$(CH_2)_2CH(CH_3)(CH_2)_2$-	Cl	H	H	CH_3	Cl	174-179
I-209	-$CH(CH_3)(CH_2)_3$-	Cl	H	H	CH_3	Cl	176-195
I-210	-$CH(CH_3)(CH_2)_3$-	Cl	H	H	CH_3	Cl	149-159
I-211	-$(CH_2)CH(CH_3)(CH_2)_2$-	F	H	Cl	CH_3	Cl	70-92
I-212	-$CH(CH_3)(CH_2)_4$-	F	H	Cl	CH_3	Cl	181-187
I-213	-$(CH_2)_2CH(CH_3)(CH_2)_2$-	F	H	Cl	CH_3	Cl	170-176
I-214	-$(CH_2)_2CH(CH_3)(CH_2)_2$-	Cl	H	NO_2	H	OCH_3	oil
I-215	-$(CH_2)_2CH(CH_3)(CH_2)_2$-	Cl	H	NO_2	H	CH_3	oil.
I-216	-$(CH_2)CH(CH_3)(CH_2)_2$-	Cl	H	Cl	CH_3	Cl	109
I-217	-$(CH_2)CH(CH_3)(CH_2)_2$-	Cl	H	F	F	Cl	129
I-218	-$(CH_2)_2CH(CH_3)(CH_2)_2$-	Cl	H	Cl	CH_3	Cl	147-148
I-219	-$(CH_2)_2CH(CH_3)(CH_2)_2$-	Cl	H	F	F	Cl	182-183
I-220	-$CH(CH_3)(CH_2)_3$-	Cl	H	Cl	CH_3	Cl	211-212
I-221	-$CH(CH_3)(CH_2)_3$-	Cl	H	F	F	Cl	225
I-222	-$CH(CH_3)(CH_2)_4$-	Cl	H	Cl	CH_3	Cl	144
I-223	-$CH(CH_3)(CH_2)_4$-	Cl	H	F	F	Cl	186
I-224	-$(CH_2)CH(CH_3)(CH_2)_2$-	Cl	H	H	CH_3	Cl	85-87
I-225	-$(CH_2)_2CH(CH_3)(CH_2)_2$-	Cl	H	Cl	F	Cl	175-176
I-226	-$(CH_2)_2CH(CH_3)(CH_2)_2$-	Cl	H	F	Cl	Cl	205-206
I-227	-$CH(CH_3)(CH_2)_3$-	Cl	H	Cl	F	Cl	191-193
I-228	-$CH(CH_3)(CH_2)_3$-	Cl	H	F	Cl	Cl	246-248

No.	R^1	R^2	Hal	L^1	L^2	L^3	X	Phys. Data (mp. [°C])
I-229	$-CH(CH_3)(CH_2)_4-$		Cl	H	Cl	F	Cl	184-186
I-230	$-CH(CH_3)(CH_2)_4-$		Cl	H	F	Cl	C	183-185
I-231	$-(CH_2)CH(CH_3)(CH_2)_2-$		Cl	H	Cl	F	Cl	oil
I-232	$-(CH_2)CH(CH_3)(CH_2)_2-$		Cl	H	F	Cl	Cl	154-156
I-233	$-CH(CH_3)(CH_2)_3-$		F	H	Cl	CH_3	Cl	194-195
I-234	$-(CH_2)_2CH(CH_3)(CH_2)_2-$		Cl	F	H	H	Cl	192-193
I-235	$-CH(CH_3)(CH_2)_3-$		Cl	F	H	H	Cl	185-187
I-236	$-CH(CH_3)(CH_2)_4-$		Cl	F	H	H	Cl	163-165
I-237	$-(CH_2)CH(CH_3)(CH_2)_2-$		Cl	F	H	H	Cl	85-86
I-238	$-(CH_2)_2CH(CH_3)(CH_2)_2-$		Cl	H	NO_2	Cl	Cl	204-207
I-239	$-CH(CH_3)(CH_2)_3-$		Cl	H	NO_2	Cl	Cl	oil
I-240	$-CH(CH_3)(CH_2)_4-$		Cl	H	NO_2	Cl	Cl	178-179
I-241	$-(CH_2)CH(CH_3)(CH_2)_2-$		Cl	H	NO_2	Cl	Cl	oil
I-242	$-(CH_2)_2CH(CH_3)(CH_2)_2-$		Cl	H	H	F	OCH_3	208-210
I-243	$-CH(CH_3)(CH_2)_4-$		Cl	H	H	F	OCH_3	128-130
I-244	$-(CH_2)_2CH(CH_3)(CH_2)_2-$		Cl	H	H	F	CN	200-202
I-245	$-CH(CH_3)(CH_2)_4-$		Cl	H	H	F	CN	220-222
I-246	$-(CH_2)_2CH(CH_3)(CH_2)_2-$		Cl	H	H	F	CH_3	169-171
I-247	$-CH(CH_3)(CH_2)_4-$		Cl	H	H	F	CH_3	168-170
I-248	$-CH(CH_3)(CH_2)_4-$		Cl	H	H	F	Cl	166-168
I-249	$-(CH_2)_2CH(CH_3)(CH_2)_2-$		F	H	F	F	Cl	200-203
I-250	$-(CH_2)_4-$		Cl	H	H	F	Cl	163-167
I-251	$-(CH_2)_4-$		Cl	H	H	Cl	Cl	157-160
I-252	$-(CH_2)_2CH(CH_3)(CH_2)_2-$		Cl	H	H	Cl	CH_3	oil
I-253	$-(CH_2)_2CH(CH_3)(CH_2)_2-$		Cl	H	Cl	H	Cl	oil

B2 Additional Use Examples

a) Greenhouse

Formulation

The active ingredients were used separately to prepare a stock solution comprising 25 mg active ingredient, which was filled up with a mixture of acetone and/or DMSO and the emulsifier Wettol EM31 (emulsifying and dispersing wetter based on ethoxylated alkylphenols) in a volume ratio solvent: emulsifier of 99 : 1 ad 10 ml solution. Afterwards water was added ad 100 ml. This stock solution was diluted with the above described solvent: emulsifier: water mixture to give the desired active ingredient concentrations stated below.

Additional Use Example 1 – Fungicidal control of early blight on tomatoes (*Alternaria solani)*

Leaves of pot grown tomato seedlings were sprayed eith an aqueous suspension containing the active compound in the concentration mentioned below. The next day the leaves were infected with a zoospore suspension of Alternaria solani (0.17×10^6 spres per ml of a 2% strength biomalt solution). The plants were then placed in a water vapour-saturated chamber at 20 to 22°C. After 5 days the isease had spread to such a great extent on the untreated plants that the fungicidal activity of the substances could be assessed.

In this test, the plants which had been treated with 250 ppm of compounds I-23, I-136, I-150, I-194, I-195, I-196, I-197, I-198, I-199, I-200, I-201, and I-253, resp., showed an infection of not more than 30%, whereas the untreated plants were infected to 90%.

Additional Use Example 2

Activity against gray mould on paprika leaves caused by *Botrytis cinera* in a one day protective application

Paprika seedlings of the "Neusiedler Ideal Elite" variety were sprayed to run-off at the two to three leave stage with an aqueous suspension containing the concentration of active ingredient mentioned below. On the following day, the plants were inoculated with a spore suspension of *Botrytis cinera* in 2 wt.-% aqueous biomalt solution. The infected plants were then incubated in chambers with high humidity at 22-24°C. After five days, the extent of fungal infection on the leaves could be assessed visually in %.

In this test, the plants which had been treated with 250 ppm of compounds I-23, I-136, I-195, I-196, I-197, I-198, I-199, I-200, I-201 and I-206, respectively, showed an infedtion of no more than 1%, whereas the untreated plants were infected to 90%.

b) Microtiter Tests

The active ingredients were prepared separately as DMSO stock solution at a concentration of 10,000 ppm.

Additional Use Example 3

Activity against gray mould caused by *Botrytis cinera*

The stock solution of the active compound was pipetted onto a microtiter (MTP) and diluted to the concentration indicated below with an aqueous fungi nutrient medium based on malt. Subsequently, an aqueous spore suspension of *Botrytis cinera* was added. The plates were then placed in a humid chamber at a temperature of 18°C and a relative humidity close to 100%. On the seventh day after inoculation, the MTPs were scanned with an absorption photometer at 405 nm.

The measured parameters were compared to the growth of the active-free control variant (100%) and the fungi-free and active-free blank value, to calculate the relative growth in % of the pathogens in the respective active compounds.

In this test the pathogens which had been treated with 125 ppm of compounds I-181, I-238, I-239, I-240, I-241, I-250 and I-252, respectively, showed a relative growth of no more than 12%.

Additional Use Example 4

Activity against rice blast caused by *Pyricularia oryzae*

The stock solution of the active compound was pipetted onto a microtiter (MTP) and diluted to the concentration indicated below with an aqueous fungi nutrient medium based on malt. Subsequently, an aqueous spore suspension of *Pyricularia oryzae* was added. The plates were then placed in a humid chamber at a temperature of 18°C and a relative humidity close to 100%. On the seventh day after inoculation, the MTPs were scanned with an absorption photometer at 405 nm.

The measured parameters were compared to the growth of the active-free control variant (100%) and the fungi-free and active-free blank value, to calculate the relative growth in % of the pathogens in the respective active compounds.

In this tests the pathogens which had been treated with 125 of compounds I-249, I-238, I-247, I-246, I-245, I-244, I-243, I-233, I-232, I-231, I-237, I-236, I-235, I-234, I-251, I-242, I-248, I-213, I-212, I-195, I-202, I-200, I-121, I-208, I-210, I-209, I-207, I-211, I-214, I-217, I-216, I-215, I-219, I-218, I-223, I-222, I-221, I-220, I-226, I-225, I-224, I-230, I-229, I-228, I-227 and I-206, respectively, showed a relative growth of no more than 6%.

Additional Use Example 5

Activity against the speckled leaf blotch pathogen *Septoria tritici*

The stock solution was pipetted onto a microtiter plate (MTP) and diluted to the stated active compound concentrate using a malt-based aqueous nutrient medium for fungi. An aqueous spore suspension of *Septoria tritici* was then added. The plates were placed in a water vapour-saturated chamber at temperatures of 18°C. Using an absorption photometer, the MTPs were measured at 405 nm on day 7 after the inoculation.

The measured parameters were compared to the growth of the active-free control variant (100%) and the fungi-free and active-free blank value, to calculate the relative growth in % of the pathogens in the respective active compounds.

In this tests the pathogens which had been treated with 125 of compounds I-249, I-238, I-247, I-246, I-245, I-244, I-243, I-233, I-232, I-231, I-237, I-236, I-235, I-234, I-251, I-242, I-248, I-213, I-212, I-195, I-202, I-200, I-121, I-208, I-210, I-209, I-207, I-211, I-214, I-217, I-216, I-215, I-219, I-218, I-223, I-222, I-221, I-220, I-226, I-225, I-224, I-230, I-229, I-228, I-227 and I-206, respectively, showed a relative growth of no more than 6%.

The additional synthesis and use examples support the scope of the claimed subject matter.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information or belief are believed to be true; and further that these statements are made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signed at 67056 Ludwigshafen, Germany, this ... day of February 2008.

Dr. Egon Haden